

## **Human cumulus cells-derived EVs and their role in the acquisition of the oocyte developmental competence**

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The communication between the oocyte and cumulus cells (CCs) affects the gamete ability to develop to the blastocyst stage. We showed that germinal vesicle (GV) mouse oocytes matured to metaphase II (MII) on a feeder layer of CCs (FL-CCs) derived from incompetent oocytes interrupt their development at the two-cell stage; instead, the blastocyst is reached when cultured on FL-CCs from competent oocytes (PMID: 30922442). We also found that FL-CCs release extracellular vesicles (EVs) containing 74 differentially expressed miRNAs (PMID: 38745364).

Here, we present the translation of this culture platform from mice to humans to identify EVs-enclosed miRNAs released by human FL-CCs (hFL-CCs). hFL-CCs were produced from patient-specific COCs classified as competent or incompetent when >30% or <30% of their oocytes reached blastocyst, respectively. EVs were isolated from the medium of the two experimental conditions, miRNAs were extracted, and the subsequent NGS analysis identified 25 miRNAs differentially expressed (19 up- and 6 down-regulated). These miRNAs are promising candidates for decoding the somatic contribution to the acquisition of the oocyte developmental competence.

We are now producing hFLs using CCs derived from individually isolated COCs, for a direct correlation between the EVs miRNA profile and the oocyte's ability to complete pre-implantation development.